THE RECOVERY CONTRACTURE IN MUSCLE; A NEW GENERAL SALT EFFECT[1]

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In a study on permeability and fatigue in muscle and its bearing on the problem of ion antagonism, the method used in a series of experiments was as follows. The sartorius muscle was stimulated for five minutes with condenser discharges about 60–90 times per minute. Thereafter the muscle was allowed to rest for at least five minutes in Ringer's solution with normal or increased Ca content and then a new series of stimulations of the same frequency was begun. The muscle was in a moist chamber when stimulated. Under these conditions a peculiar phenomenon was observed. In the beginning of the second stimulation series the muscle showed a contracture which became less during the continuation of the stimulations and finally disappeared more or less completely. The phenomenon is fundamentally different from the fatigue contracture in muscle which increases with the continuation of stimulations. The experiments described below serve to analyse the phenomenon.

Method

The experiments were carried out on m. sartorius and biceps of *Rana esculenta*. The carefully prepared muscles were suspended between platinum electrodes and stimulated by means of the apparatus of Scheminsky, which allowed one to use condenser discharges over a wide range of frequencies. The strength of the stimulus was varied by a parallel resistance; there was also a resistance of 10,000 ohms in series in order to make very slight changes in the conductivity of the muscle ineffective. The stimuli were either just maximal or submaximal. The muscles were loaded with 2 g; the magnification of the isotonic lever was six fold. The experiments were performed from October 1930 to January 1931.

Results

I. The Basic Phenomenon

A typical example is reproduced in Fig. 1. In this experiment the sartorius was stimulated 90 times per minute with a condenser of 0.5 mf. Between the periods of stimulation the muscle recovered in a

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well-aerated Ringer's solution. Each period of stimulation and recovery lasted for five minutes. One recognizes from Fig. 1 that the curves *b*–*d* show in the beginning contractures which decrease while stimulation is being continued. There is a regular decrease in the

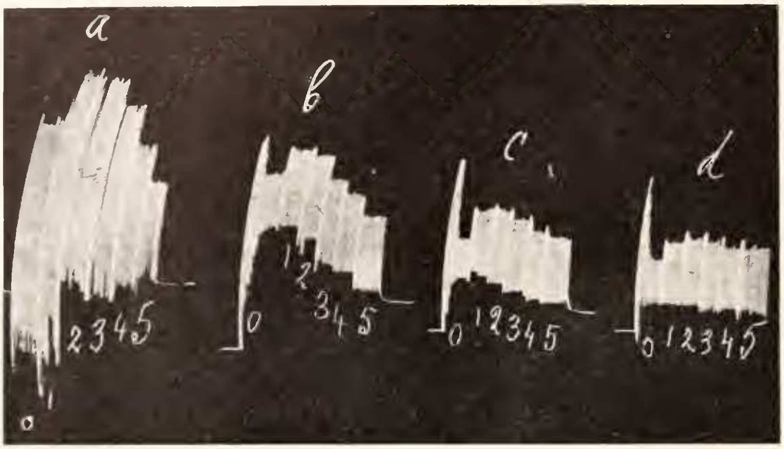

Fig. 1. Four stimulation periods on sartorius. Condenser discharges (0.5 mf.) 90 times per minute, in a moist chamber. Muscle is in Ringer's solution during recovery period. The conditions in all succeeding experiments are the same unless otherwise specified

height of contracture from *b* to *d*.[2] This makes it plain that the phenomenon in question is basically different from the fatigue contracture since (1) fatigue contracture increases with the continuation of stimulation and (2) in spite of a slight decrease in the height of contractions from *b* to *d*, *i.e.*, an increase in fatigue, the contracture becomes less. This peculiar behavior of the contracture makes it rather probable that it might be due to a recovery and not to a fatigue process. As to the height of contractions, it is characteristic that although the contractions decrease in the very beginning of the contracture until the maximum of the contracture has been reached, hereafter a remarkable increase in the height of contractions is accompanied by a decrease in contracture.

There are still other facts which support the hypothesis that the phenomenon is a recovery contracture. It is known that with increasing fatigue the duration of the contraction increases. The detailed study has shown that the change in duration chiefly concerns relaxation. At first one may see that an elastic vibration ends the

[2] In the text and in the figures the different stimulation periods are designated as *a*, *b*, *c*, *d*. The first which can show recovery contracture is the *b* curve.

period of relaxation. With increasing fatigue the elastic vibration disappears and a slow contraction (designated as "Funke's Nose") is apparent in the downstroke of the contraction. The more fatigue progresses the earlier in the downstroke appears this slight contraction. Since the relaxation period of the "Funke's Nose" is much longer than in a normal contraction the duration of the contraction increases in correspondence with the earlier appearance of the "nose." The registration of the recovery contracture on a faster revolving drum revealed the interesting fact that the changes described as characteristic for fatigue (Funke, Wachholder) also occur during the recovery contracture but in the *reverse order* as is shown in Fig. 2, in which tracings obtained at intervals of one minute are recorded.

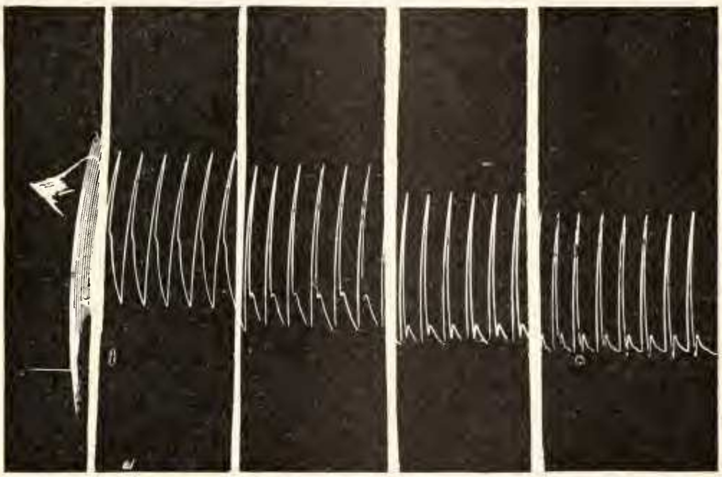

FIG. 2. *b*-curve on a faster moving drum.

It was stated above that the recovery contracture decreases with increasing number of alternating stimulation and recovery periods as is apparent if the recovery contracture in Fig. 1, *b* is compared with 1, *c* or 1, *d*. Experiments on a fast revolving drum revealed that the changes in shape and duration of the contraction correspond to simultaneous changes in the size of contracture. In an experiment, for instance, which was carried out in a similar manner as that reproduced in Fig. 1, it was found that the disappearence of the "Funke's Nose" required one minute in experiment *d*, four minutes in experiment *c* and more than five minutes in experiment *b*. In other words, the recovery phenomenon judged in its intensity according to the height of contracture and to the time during which the "Funke's Nose" appears decreases the more the fatigue increases. That is, of course, to be expected, since recovery is more marked in a slightly fatigued muscle than in one which has been very much fatigued. Thus the phenomenon is undoubtedly a recovery contracture and the question arises as to what factors are responsible for its occurrence.

II. The Influence of Strength, Frequency, and Duration of Stimuli on the Occurrence of Recovery Contracture

Systematic studies showed that the recovery contracture is rather independent of the strength of the stimuli since it occurs in experiments with submaximal as well as maximal condenser discharges. This makes it plain that the contracture is different from Tiegel's contracture, which requires the application of supermaximal currents. However, the frequency of stimulation had a marked influence. Experiments were carried on in which the frequency of stimuli in the first and second periods varied independently over a range of from 30 to 150 per minute. It was apparent that at least 45 stimulations were required in the first period to bring about the contracture in the second, provided that during this period the frequency was at least one hundred. Under these conditions, the higher the frequency employed in the second period, the more marked the contracture. But this is true only up to a frequency of 120 per minute, since beyond this value the contracture dropped slightly. It is easily understandable that stimulations below 45 per minute during the first period did not produce a recovery contracture in the second even if very high frequencies were used, since under these conditions in the first period no fatigue was observed. Therefore, a recovery phenomenon must fail to appear.

In general it may be said that the higher the frequencies used in both periods, the more marked the recovery. But even after a first period of high frequency the contracture does not occur unless the mus-

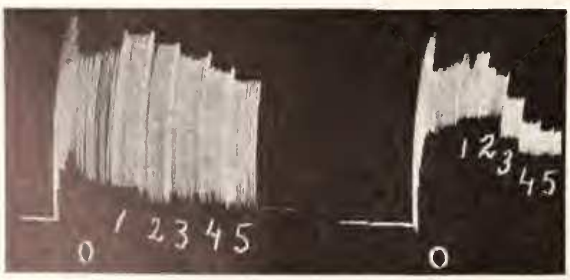

Fig. 3. *b* curve in two sartorii of the same frog. Frequency of stimulation in the first *b*-curve 60 per minute; in the second, 120 per minute.

cle is stimulated at least 45 times per minute in the second period. The strength of the recovery contracture is not only apparent in its height but also in the changes in the shape and duration of the contraction. This may be illustrated by Figs. 3 and 4. In Fig. 3 the recovery contracture of two sartorii of the same frog are reproduced. The frequency during the first period was the same in both cases (90 per min-

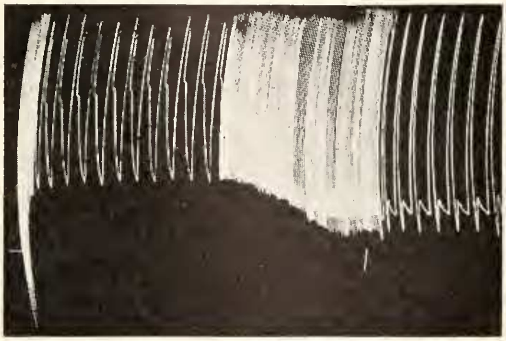

FIG. 4. *b*-curve. Frequency in *a*-curve was 60; in *b*, 90 per minute.

ute), while in the second period the first muscle was stimulated 60 times and the second muscle 120 times per minute. Fig. 4 shows that the "Funke's Nose" disappears in the downstroke of the contraction within one minute, frequency of stimulation being 60 in the first and

FIG. 5. *b*-curve. The two sartorii were stimulated in the *a* period with a condenser 0.1 mf.; in the *b* period of the first muscle a condenser of 2.0 mf. was used, in that of the second a condenser of 0.1 mf.

90 in the second period, while if during both periods the muscle is stimulated 90 times per minute, it takes much longer for the duration of contraction to become normal. (Compare Fig. 2.)

The duration of the stimulus also seems to affect the recovery contracture. In Fig. 5 the recovery contracture of two sartorii of the same frog is reproduced from an experiment in which strength and frequency of the stimulus were identical, but the duration of the stimulus was in the first muscle 70σ and in the second 20σ. One recognizes in Fig. 5 that increasing duration of the stimulus increases recovery contracture. But even with very short currents the phenomenon can be observed, since recovery contracture is obtained in sartorius after application of submaximal induction currents. It also shows under these conditions the characteristic features mentioned above which concern the occurrence of the "Funke's Nose" and the duration of the single contraction.

III. The Influence of Salts and Non-electrolytes on the Occurrence of Recovery Contracture

This paragraph deals with the problem of the physico-chemical factors which determine the occurrence of the recovery contracture. In the first group of experiments one muscle recovered in the moist chamber while the other muscle of the same frog recovered in Ringer's solution as in the previously described experiments. In order to get

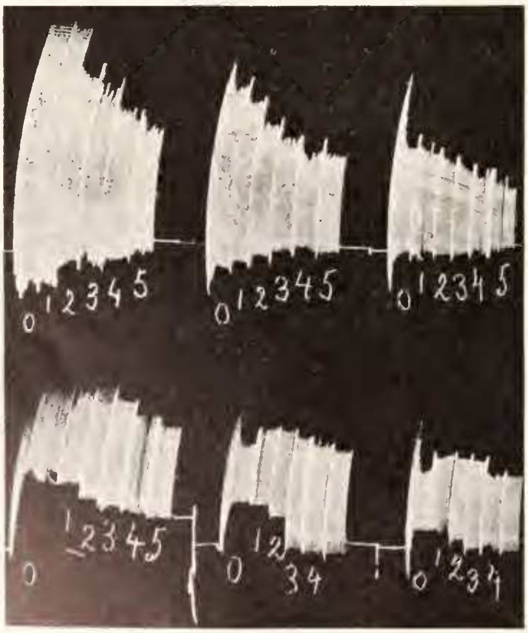

Fig. 6. *b–d* curves of two sartorii of the same frog. Upper tracing: recovery period in moist chamber. Lower tracing: recovery period in Ringer's solution.

distinct results it is advisable to avoid soaking the muscle in Ringer's solution for a long time when it is afterwards to be in the moist chamber during the recovery period.

Dulière and Horton observed recently that a muscle which is brought into a moist chamber without having been in contact with Ringer's solution lost its irritability. The observations of these authors were confirmed and therefore the muscle was immersed in Ringer's solution for two minutes before being placed in the moist chamber. Under these conditions the irritability of the muscle did not change and the very striking result was regularly obtained that the muscle which recovered in a moist chamber did not show recovery contracture, while the muscle immersed in Ringer's solution during recovery period always showed the contracture. Figure 6 gives an illustration of the

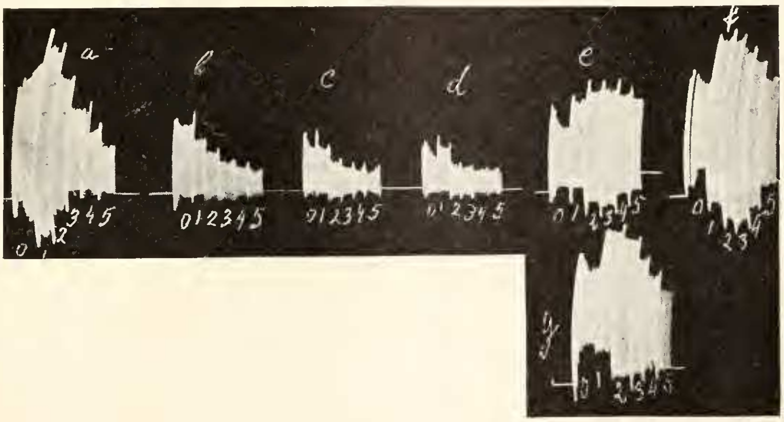

FIG. 7. *a–g* curves of sartorius. Between *a* and *d* period, muscle in moist chamber; between *d* and *g*, in Ringer's solution during recovery.

typical results for three periods (*b-d*). While the "Ringer" muscle undergoes the typical recovery contracture, decreasing more and more with each stimulation period, the "air" muscle does not show any contracture.[3] The change in the shape and duration of the contractions is also restricted to the muscle which recovered in Ringer's solution and showed recovery contracture.

Experiments of this type were performed in great number without a failure. It is interesting to note that, as Fig. 7 indicates, alternating conditions bring about alternate presence and absence of the contrac-

[3] For the sake of brevity the muscle which remained in Ringer's during the recovery period is referred to as the "Ringer muscle," that which remained in the moist chamber, the "air muscle."

ture of the muscle. In this experiment the muscle remained during the first three recovery periods in a moist chamber and therefore did not show a recovery contracture; after the fourth stimulation period it always remained in Ringer's solution during the recovery period. The effect is very significant. The long period in air influenced the behavior of the muscle so that one recovery period in Ringer's did not immediately bring about the contracture. Therefore it is not noticeable in experiment *e*, but it becomes apparent in *f* and still more in *g*.

The time during which the muscle was kept in Ringer's solution before the experiment was started is not immaterial to its reaction in reference to the recovery contracture. Thus it was found that soaking the muscle for 24 hours in Ringer's solution increases its tendency to react with recovery contracture even if the muscle is kept in a moist chamber during the recovery period. This may be illustrated by Fig. 8. The first curve showed a typical although very slight recovery

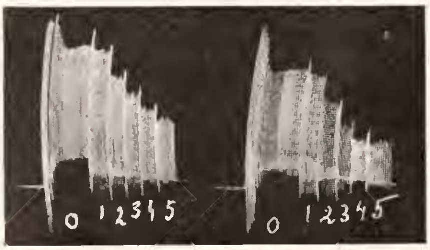

FIG. 8. Both sartorii soaked for 24 hours in Ringer's solution. First muscle immediately thereafter stimulated as in Fig. 1, the second muscle remained one hour in moist chamber before stimulation. Muscles in moist chamber during recovery period. *b*-curves reproduced.

contracture. But the contracture was still smaller in the second sartorius of the same frog, which was held in a moist chamber for one hour before starting the stimulation. It was, of course, also soaked for 24 hours in Ringer's solution. Besides, the second muscle shows but a slight decrease in the elastic vibrations during contracture while the first one did not show them at all. This indicates, as was proven by registering on a fast revolving kymograph, that in the first case the contracture was accompanied by the occurrence of the "Funke's nose," which did not occur in the second case. Summing up these observations, it may be said that recovery contracture occurs if the muscle is kept in Ringer's solution during the recovery period and it disappears if the muscle is in a moist chamber during that period. The effects are reversible. The soaking of the muscle in Ringer's solution furthers the recovery contracture.

Seeking for an explanation of this peculiar phenomenon it seemed rather probable that the presence or absence of the contracture might be due to differences in ion concentrations at the surface layer of muscle, since the efficiency of ions to produce contractures and influence the "tonus" of muscles is known (Neuschlosz, Gellhorn). But experiments did not prove the correctness of this view. The recovery contracture occurs not only if the muscle is kept in Ringer's solution but also if the composition of that solution is much altered. An increase in the K or Ca concentration to ten times its original value did not noticeably influence the strength of the recovery contracture. The phenomenon was also observed in isotonic NaCl, Na_2SO_4 and LiCl solutions. If the K or Ca content of the muscle were responsible for the phenomenon in question, changes in concentration of these ions should be effective. Therefore it was thought that one might have to do here with a general salt effect as was first observed by Loeb (for further references compare Gellhorn, 1926 and 1929, pp. 153–163). In this case the contracture should be diminished or should not occur at all if the muscle were placed in a non-electrolyte solution during the recovery period. In fact, the experiments carried out with glucose, sucrose and urea either alone, in isotonic solution or replacing different

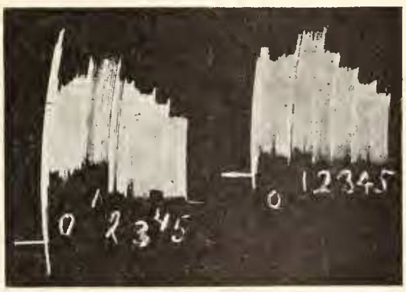

FIG. 9. *b*-curves. (m. sartorius.) Muscle 1 in Ringer's, muscle 2 in 3 cc. Ringer's + 17 cc. isotonic urea during recovery period.

parts of Ringer's solution, yielded the expected results. Figures 9 and 10 show a typical experiment on sartorius and biceps. In Fig. 9 the recovery contracture was much decreased if the muscle remained in a solution consisting of Ringer's + urea during the recovery period. In Fig. 10 it is shown that recovery contracture is suppressed completely if the muscle is immersed in isotonic sucrose solution during the recovery period.[4]

[4] In some of the experiments it was observed that the sartorious muscle showed a small contracture when immersed in isotonic non-electrolyte solutions. Therefore in most cases mixtures of Ringer's and non-electrolyte solutions were employed which did not produce a contracture during the recovery period.

As mentioned above, the experiments were carried out on the sartorius and biceps of *Rana esculenta*. The results were the same in both muscles. This seems of interest in respect to observations of Sommerkamp, who found that some groups of muscles react more to reagents which produce contractures, especially to acetylcholin, than others. This fact was explained by structural differences because the

FIG. 10. *b*-curves. (m. biceps.) Muscle 1 in Ringer's, muscle 2 in isotonic sucrose during recovery period.

content of "tonusfibers" is different in different muscles. The observations of this paper seem to indicate that in the recovery contracture only the ordinary muscle fibers are involved since biceps and sartorius behaved rather alike in spite of the differences observed by Sommerkamp in experiments with acetylcholin.

As to the explanation of the recovery contracture, several facts support the assumption that the condition of the surface layer of the muscle is the determining factor for its appearance. This is not meant in the sense of the theory of Botazzi, who believes that sarcoplasm is responsible for "tonic" reactions, but there are a number of observations which show more or less the dependence of contractions and contractures upon the surface layer of the muscle cell and its permeability. It will be recalled that fatigue in muscle can be delayed by an excess of calcium in Ringer's solution (Gellhorn), and furthermore, that K and SCN contractures depend entirely on permeability (Gellhorn).

The importance of the behavior of the surface of muscle for the recovery contracture is expressed by two groups of observations: 1. It was shown that the recovery contracture is increased by the application of condenser discharges with relatively long duration of discharge. As was recently proved by v. Gulacsy and Heller such discharges bring about marked polarisation phenomena on the surface layer of muscle. 2. Experiments were described demonstrating that the recovery contracture was diminished or suppressed in the presence of non-electrolytes. This shows that a general salt effect is present as in the experiments of Loeb. It still remains a question as to whether the same process underlies the salt effect in Loeb's and in our own observations. But the experiments seem to point out that the conditions of the colloids in the surface layer of the cells are different when recovery contracture occurs and when it is prevented.

Summary

If the sartorius or biceps of *Rana esculenta* is stimulated with condenser discharges in periods of five minutes with a frequency varying between 45 and 150 per minute and stimulation periods alternate regularly with recovery periods of the same duration, a recovery contracture is brought about in the beginning of the second and each following stimulation periods provided the muscle is allowed to recover in an aerated salt solution. Wide changes in the K and Ca concentration of the Ringer's solution are without influence. The contracture also occurs when isotonic solutions of Na or Li salts are employed. The phenomenon is suppressed by replacing the salt with a non-electrolyte. The following observations are in favor of the assumption that the contracture is a recovery contracture:

1. The phenomenon does not occur if the frequency is too low to produce even a slight fatigue.
2. It decreases from the second to the fourth stimulation period, *i.e.*, with increasing fatigue.
3. The changes in the shape of the contractions (Funke's Nose) during the recovery contracture show a temporal sequence just the opposite of that in fatigue.

It is assumed that changes in the surface layer of the muscle cell bring about the recovery contracture. In favor of this hypothesis are the facts:

1. The recovery contracture is increased with increasing duration of the electrical discharges which were used to stimulate the muscle.
2. Non-electrolytes which suppress the phenomenon bring about changes in the surface layer of cells.

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